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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER
WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
1632	11

DATE MAILED: 06/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary

Application No.	Applicant(s)
09/743,544	Farris, R.
Examiner	**Art Unit**
Joseph Woitach	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 27, 2003*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *35-41 and 49-64* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *35-41 and 49-64* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This application is a 371 national stage filing of PCT/US99/15625, filed July 8, 1999, which claims benefit of 09/113,774, file July 10, 1998, now US Patent 6,129,911.

Applicant's amendment filed March 27, 2003, paper number 10, has been received and entered. The specification has been amended. The abstract has been added. Claims 1-34 and 42-48 have been canceled. Claim 35 has been amended. Claims 49-64 have been added. Claims 35-41 and 49-64 are pending.

Election/Restriction

Applicant's election without traverse of group III, claims 35-41, drawn to a method of obtaining isolated liver stem cells, in Paper No. 6 was acknowledged. Newly added claims 49-64 are dependent claims depending directly or indirectly to claim 35 and are encompassed by the elected invention. Accordingly, claims 35-41 and 49-64 are currently under examination.

Priority

Applicant has complied with the requirements of 37 CFR 1.78(a)(2) and (a)(5) for receiving the benefit of an earlier filing date.

The amendment to the first line of the specification reciting the priority information has perfected the priority claim.

Oath/Declaration

As indicated in the previous office action, the oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

It is noted that declaration was amended to indicate the Inventors new address as of 12/25/01, however it is unclear when this amendment was made. The Inventor signed the declaration 4/23/01, however he did not initial the change of address.

Drawings

It is noted that formal drawings will be required if the application is allowed.

Specification

The abstract of the disclosure is in accordance with 37 CFR 1.52(b)(4).

The addition of the abstract made in Applicants amendment filed March 27, 2003, has obviated the basis of the objection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 35-41 and 49-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Initially, the amendment of claim 35 to delete the limitation "said doublet" in step (c) has obviated the basis of the previous rejection.

Claim 35 is unclear in the recitation of "substantially pure liver stem cells" because the method as amended results in clusters of 2-5 cells not a pure population of liver stem cells. It is noted the that specification defines 'substantially pure" when the *stem cell or doublets* are at least 60% of the cell population (page 4, lines 20-25, *emphasis added*), however if one follows the method as instantly claimed it does not appear that the isolated population will contains 60% doublets or stem cells. Even if the composition is 100% doublets, then the greatest amount of stem cells would be 50% which would not fall under the definition of 'substantially pure' set forth in the disclosure. Additionally, the claim appears incomplete because it is a method of obtaining pure liver stem cells, however only clusters of cells result from practicing the method. Finally, it is unclear if the cluster consists of 2-5 stem cells or 2-5 cells in total. Both hepatocytes and stem cells are considered cells, and it is unclear to what the specific number refers, stem cells, hepatocytes, or total cells. Dependent claims are included in the basis of the rejection

because they fail to further clarify the basis of the rejection, only setting forth specific sources of liver or specific antigenic markers. More clearly setting forth method steps that result in a substantially pure population of liver stem cells would obviate the basis of the rejection.

Claim 36 is vague and unclear on how the recited method step is related to isolating liver stem cells as set forth in claim 35. It is unclear when, how or why periportal hepatocytes are isolated and how this is related to pure liver stem cells or isolation of the clusters. More clearly setting forth method steps that result in a substantially pure population of liver stem cells would obviate the basis of the rejection.

Claims 39-40 are vague and unclear to when the specific method steps are practiced in relationship to the method set forth in claim 35. It is unclear if it used to isolate a liver stem cell or to isolate the cluster. Further, it is noted that claim 40 recites using the antigen OV6 which required by the method of claim 35.

Claim 49 is unclear and confusing because it appears not further limit claim 35, and simply terms a liver stem cell as a pre-oval cell. It is unclear is a liver stem cell is a population of different types of cells including a pre-oval stem cell, or how terming the stem cell as a pre-oval cell further limits the liver stem cell which was isolated. Upon review of the specification it appears that a liver stem cell is considered a pre-oval cell based on its location in the liver and its ability to give rise to an oval cell, thus does not further limit claim 35.

Claims 58-60 recites the limitation "said sample", however there is insufficient antecedent basis for this limitation in the claim or in independent claim 35 from which it

depends. Further, the claim is confusing because as discussed above for claim 35, even if one were to interpret the claim to encompass 100% doublets, the resulting number of liver stem cells would not be substantially pure being lower than 60% as defined in the specification.

Claims 61-64 are confusing because removing the hepatocytes from the clusters should only leave stem cells wherein the population is 100% pure. The method is unclear because how one would obtain a population less than 100% after removing the hepatocytes from the cluster is not clearly set forth in the claim nor the specification. It is unclear how removing one of two types of cells present in the cluster would result in populations which are 60%, 90% or 99% stem cells, or how practicing this step would result in these specific selected percentages.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 35-38 rejected under 35 U.S.C. 102(b) as being anticipated by Reid *et al.* (WO 93/03142) is withdrawn.

Claims 35-38 are drawn to a method of obtaining a liver stem cell comprising isolating a cluster of cells from the liver and separating the hepatocytes from the stem cell and have been

amended to indicate the size and nature of the cluster isolated by the method. Reid *et al.* does not specifically teach this cluster size or the specific markers recited in the claims. In light of the claim amendments, the rejection is withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 39-41 rejected under 35 U.S.C. 103(a) as being unpatentable over Reid *et al.* in further in view of Sell (Cancer Research, 1990) and Alison (Current Opinions in Cell Biology, 1996) is withdrawn.

Claims 35-38 have been amended to indicate the size and nature of the cluster isolated by the method. Reid *et al.* does not specifically teach this cluster size or the specific markers recited in the claims, and the addition of Sell and Alison fails to remedy this deficiency. In light of the claim amendments, the rejection is withdrawn.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 35-41 stand rejected and newly added claims 49-64 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 35-44 of U.S. Patent No. 6,129,911 ('911). Although the conflicting claims are not identical, they are not patentably distinct from each other because the method set forth in the patent is encompassed by the instant claims.

Applicant has not specifically addressed the double patenting rejection made in the previous office action. As note in the previous office action, the metes and bounds of what is considered a cluster of cells is specifically defined in the specification. The claims '911 patent recites that the cluster is less than 10 cells, however dependent claim 37 indicates that the cluster is comprised of only a doublet which is the same limitation recited in claim 37 of the present application. In view of the minimum limitation of a cell doublet, and in view of the teaching of each of the specification for a cell cluster, any higher range limit would be considered an obvious variant as long as at least the doublet is present. With respect to the limitations of specific markers these are set forth in dependent claims are exactly the same in both claim sets. The tissue source and level of purity do not represent any novel or unobvious limitation since the cells are present in the liver and the method results in a pure population of stem cells.

Conclusion

No claim is allowed. The claims are free of the art of record because the art fails to teach or suggest the isolation of cell clusters of 2-5 cells from the liver wherein the cells comprise the OV6 marker and do not comprise the OC2 marker. However, the claims are subject to other rejections.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Joseph T. Woitach

Deborah Crouch
DEBORAH CROUCH
PRIMARY EXAMINER
GROUP ~~1800~~ 1630